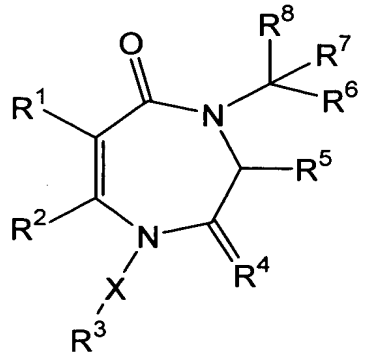
SUBSTITUTED 1,4-DIAZEPINES AND USES THEREOF

ABSTRACT

The present invention is directed to novel 1,4-diazepines, pharmaceutical compositions thereof, and the use thereof as inhibitors of HDM2-p53 interactions. Compounds have Formula *I*:



I

or a solvate, hydrate or pharmaceutically acceptable salt thereof; wherein:

R^1, R^2, R^9, R^{10}, R^a, R^d and M are defined herein;

X is a bivalent radical of: an alkane, a cycloalkane, an optionally-substituted arene, an optionally-substituted heteroarene, an optionally-substituted arylalkane or an optionally-substituted heteroarylalkane; and

R^3 is $-CO_2R^d$, $-CO_2M$, -OH, $-NHR^d$, $-SO_2R^d$, $-NHCONHR^d$, optionally-substituted amidino or optionally-substituted guanidino;

or R^3–X– is hydrogen or an electron pair;

R^4 is oxygen or $-NR^9R^{10}$;

R^5 is cycloalkyl, aryl, heteroaryl, cycloalkylalkyl, aralkyl, heteroarylalkyl, or a saturated or partially unsaturated heterocycle, each of which is optionally substituted; and

R^6, R^7 and R^8 are independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, a saturated or partially unsaturated heterocycle, cycloalkylalkyl, aralkyl or heteroarylalkyl, each of which is optionally substituted; or R^6 and

R^7, together with the carbon atom to which they are attached form a 3- to 7-membered carbocyclic ring optionally substituted 1 to 3 times with R^a.